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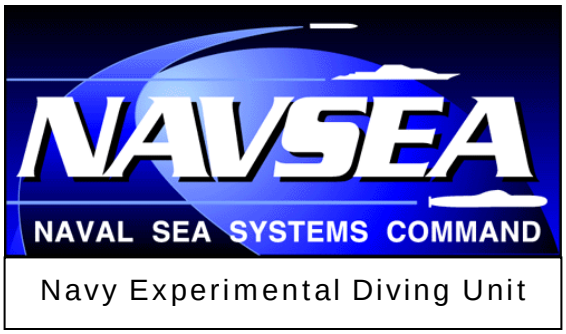
PULMONARY OXYGEN TOXICITY WHEN PARTIAL PRESSURE IS 2 ATM (200 kPa)



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14. ABSTRACT

Even asymptomatic exposures to elevated oxygen partial pressure (PO2) can influence subsequent exposures. A model previously presented predicts accumulation of pulmonary effects after exposures to PO2 = 140 kPa (1.4 atm). However, that model cannot be used with oxygen –accelerated decompression or after deep excursions. Dry chamber exposures to PO2 of 200 kPa (2 ATA on 100% humidified O2) were conducted to examine cumulative effects at PO2 more representative of those scenarios. Experiments were single (n=27), or paired three-hour exposures with surface intervals (SI) 15 to 17 hours (n=31), six hours (n=33), or three hours (n=36); single two-hour dives (n=12) had had no incidence of pulmonary oxygen toxicity. A set (n=27) of three, 30-minute dives with two-hour SI was also assessed. Flow-volume loops and diffusing capacity and symptoms were recorded before and after exposures. Significant ($p<0.05$) mean changes from baseline in pulmonary function indices after second exposures occurred immediately after surfacing for all SI and persisted for two days for three-hour SI and for one day for 15-hour SI. Incidences of symptoms were 15% immediately after one exposure and 28%, 38%, and 31% immediately after a second with 15-, six-, or three-hour SI, respectively; and those of changes in pulmonary function indices (ΔPF) were 5%, 11%, 12%, and 14% for single exposures and 15-, six-, or three-hour SI, respectively. After the third 30-minute dive, 7% of subjects had symptoms or ΔPF. Two days following the second exposure, resolution of symptoms was incomplete after six- or 15-hour SI, as was resolution of ΔPF after 15-hr SI. The incidences indicate nonlinear superposition of effects of a first and second exposure, are not readily explained by delayed-onset injury, and are not amenable to treatment like that for the 140 kPa model.

15. SUBJECT TERMS

TR 13-02; lungs, pulmonary, Oxygen toxicity, oxygen dives, hyperbaric chamber, 2 bar, pulmonary function

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INTRODUCTION

Any exposure to elevated oxygen partial pressure, even one that is asymptomatic, causes oxygen stress which takes time to resolve. A new dive will be complicated by a previous exposure unless the surface interval (SI) is long enough to ensure that the effects have resolved completely even though slow accumulation may not be evident. Many technical and military divers breathe elevated oxygen partial pressures underwater. They would benefit from knowledge of how pulmonary effects of deep excursions with 100% oxygen or of oxygen-accelerated decompression accumulate.

Accumulating pulmonary effects apply also to clinical hyperbaric treatments. For example in one study, after daily standard hyperbaric oxygen (HBO) treatments, 90 minutes at oxygen partial pressure (PO_2) 240 kPa (2.4 atm) with air breaks every 30 minutes, no significant changes in pulmonary function were found after seven days, but after 14 and 21 days, progressive decreases were noted in parameters of forced expiration, and some patients developed coughs (1). In another study with a different sequence of air breaks, ten days of 90-minute HBO treatments at 250 kPa provoked changes in forced expiratory flow indices associated with small airway function (2). However, a third study with HBO treatments at 240 kPa continuously for 90 minutes a day, five days per week for six weeks did not provoke changes in measured pulmonary function indices (3).

Knowledge of recovery time and of the residual pulmonary effects during recovery after exposures to elevated PO_2 would help in planning multiple dive missions while controlling the risk of pulmonary oxygen injury. No current models permit the estimation of recovery times after exposure to more than one PO_2.

We have previously described recovery from in-water dives with PO_2 between 130 and 140 kPa in terms of residual oxygen time, and estimated the probability of pulmonary symptoms or of changes in pulmonary function (ΔPF) (4). This study addressed recovery time after exposures to PO_2 = 200 kPa. The plan was to measure residual times through cumulative effects with a second dive. Different SI provided a range of recovery times. SI were chosen to be multiples of dive duration based on the recovery rate relationship found at PO_2 = 140 kPa. Short dives with a two-hour SI were also conducted because a two-hour SI is considered sufficient recovery time for central nervous system oxygen toxicity (5).

Pulmonary effects of oxygen are similar, wet or dry (6). Thus, dry chamber exposures were used because they have a much lower risk of central nervous system (CNS) oxygen toxicity than do those in the water; after more than 20,000 hyperbaric treatments at one facility, seizure rate was 0.03% (7). Pulmonary oxygen toxicity resulting from exposures to 200 kPa of oxygen and its time course for recovery, particularly in connection with any cumulative effects, are described.

METHODS

DIVES AND MEASUREMENT

Participants were active-duty Navy divers from Navy Experimental Diving Unit (NEDU), from other commands in the geographic vicinity of NEDU, and from Naval Reserves Great Lakes. Divers were permitted to participate multiple times, and each exposure was treated as an independent dive. The protocol was approved by the Navy Experimental Diving Unit Institutional Review Board, and divers gave written informed consent.

The experiments were single exposures or pairs of exposures with surface interval (SI) equal to the dive duration, SI of twice the dive duration, or SI five to six times the dive duration (overnight after an afternoon dive). Single exposures had to be long enough to provoke some symptoms and some measurable decrease in pulmonary function. The preliminary single dives were single two hour exposures, and subsequent exposures were three hours in length. The exposure and testing scheme for the three-hour dives is shown in Figure 1. Three, 30-min dives with two-hour SI were also conducted.

Table 1.
Diver characteristics by dive set, median (minimum–maximum)

Dive	Number	Age (yrs)	Height (cm)	Weight (kg)
One 2-hour	12	37 (20–62)	175 (170–193)	93 (75–116)
One 3-hour	27	36 (20–51)	175 (145–191)	84 (67–113)
Two 3-hour SI=3 hours	36	39 (20–62)	178 (168–188)	86 (67–109)
Two 3-hour SI=6 hours	33	35 (19–56)	178 (168–188)	91 (71–111)
Two 3-hour SI=15 (n=18) or 17 (n=12) hours	30	37 (20–50)	178 (168–191)	91 (71–111)
Three 30-minute SI = 2 hours	27	35 (27–55)	183 (168–191)	89 (71–114)

Experiments were performed in the treatment chamber at NEDU. Up to four divers plus one tender sat in the dry chamber, which was pressed on air to 200 kPa. Divers then donned hoods (Amron 8891, Vista CA) to breathe humidified, 100% O_2 open circuit for the duration of the exposure. Tenders breathed chamber air. Movies, cards, or books provided distraction. Divers were asked about symptoms of central nervous system (CNS) and pulmonary oxygen toxicity once per hour while in the chamber. At the end of the exposure time divers removed their hoods to breathe chamber air, and the chamber was surfaced.

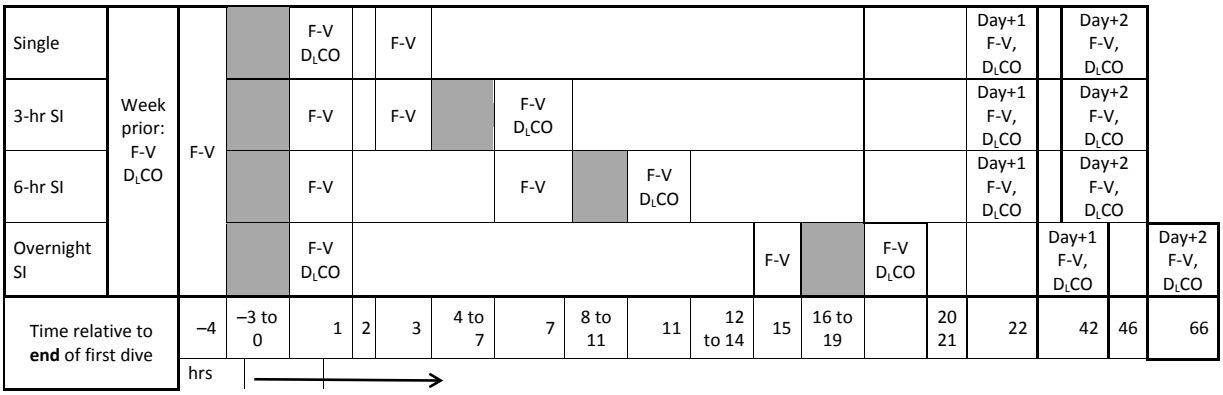

Figure 1. Time scheme of three-hour exposures relative to the first dive. Gray blocks indicate three-hour chamber exposures. Distance on the figure is not proportional to time.

Pulmonary function was measured (CPL, nSpire Medical, Longmont CO) within the week before diving, immediately before divers entered the chamber for each exposure, immediately after surfacing, two hours after the end of single exposures, and on the two days following each dive evolution. Forced flow-volume loops were measured at every session, but single breath diffusing capacity of the lungs for carbon monoxide (D_LCO) was recorded only in the week before diving, after the last exposure of the day, and on the two follow-up days (Fig. 1). The goal for every pulmonary function measurement session was three measurements that satisfied the ATS criteria (8), but no more than eight attempts were made for flow-volume loops, and no more than three for D_LCO. Valid test results were averaged. Baseline values of D_LCO came from the measurements made in the week before diving, and those for flow-volume parameters were the mean from the week before diving and from immediately before the first exposure of the series. Differences from baseline were assessed.

Flow-volume variables of interest were forced vital capacity (FVC), forced expired volume in one second (FEV_1), and forced expired flow between 25% and 75% of volume expired ($FEF_{25–75}$). D_LCO was corrected for hemoglobin and carboxyhemoglobin concentrations (9). A one-liter gas sample was used for calculations, with sample timing chosen to ensure measurement during steady-state portions of the gas concentration record. Divers were asked to fill out a symptoms questionnaire every time that pulmonary function was measured. Respiratory symptoms of interest were cough, inspiratory burning, chest tightness, and dyspnea. To rule out hyperoxic myopia, visual refraction was checked (Humphrey model 599, Carl Zeiss Meditec; Dublin, CA) at any session that included D_LCO.

ANALYSIS

Effects of time on average changes from baseline of FVC, FEV_1, $FEF_{25–75}$, and D_LCO were assessed by repeated measures ANOVA individually for each variable and SI; variables were treated as independent, and thus no correction for multiple comparisons was made. Individual comparisons within subjects were made using orthogonal contrasts which, as independent, uncorrelated measures, do not increase the Type I error rate. Additionally, pulmonary function measurements related to a first exposure were combined across different SI series when the measurements were made at the same time after surfacing (Figure 1), and effects of time were assessed using one-way ANOVA for each variable individually, and Bonferroni corrections for individual comparisons. Results were considered significant if $p<0.05$, but calculated probabilities are listed.

Individuals may experience pulmonary oxygen toxicity even when mean values of pulmonary function indices do not differ from baseline. Any measure of pulmonary function was considered to show a decrement from baseline (ΔPF) if it decreased by more than the established normal variability: 7.7% for FVC, 8.4% for FEV_1, 17% for FEF_{25-75}, and 14.2% for D_LCO (10). A subject who had one or more ΔPF at any measurement session or who reported one or more symptoms was considered to manifest pulmonary oxygen toxicity. Incidences of symptoms and of ΔPF at different times were compared using Fisher's Exact Test, when again $p<0.05$ determined significance.

To compare the exposures to PO_2 = 200 kPa with those to 130 kPa, the relations between fractions of divers with measurable pulmonary oxygen toxicity and exposure time at PO_2 = 130 kPa were used (4):

$$\% \text{ with symptoms } (\%) = 9.4 \cdot T_e - 25;$$
$$\% \text{ with } \Delta PF \ (\%) = 6.8 \cdot T_e - 22.$$

The equivalent time (T_e) expressed at PO_2 = 130 kPa was calculated from these equations.

RESULTS

MEAN CHANGES

No significant changes in the selected indices of pulmonary function were seen immediately after single 2-hour exposures, though FVC was depressed by 2.0% and FEV_1 by 2.3% on the first day after the 2-hour exposures (Figure 2). However, as none of twelve subjects reported symptoms or showed measurable ΔPF, two hour exposures with PO_2 = 200 kPa were considered too short for estimation of residual oxygen time. Further work used three-hour exposures.

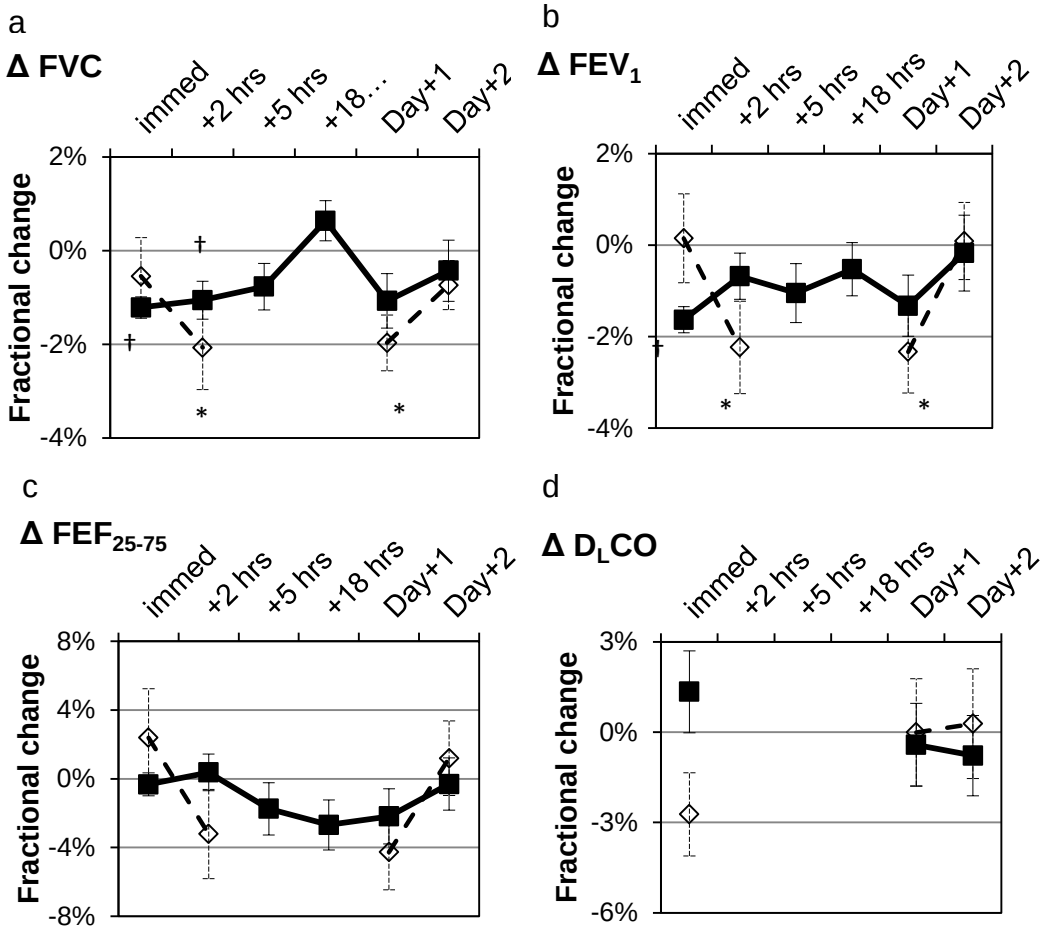

Figure 2. Changes from baseline as functions of time after single exposures, means and standard errors ——, ■: 3 hour exposure. – – ◊: two hour exposure. Differences from baseline ($p<0.05$): *: two-hour dive, †: three hour dive.

Immediately after single three-hour exposures, mean FVC, FEV_1, and $FEF_{25–75}$ were slightly but significantly depressed (FVC: –1.2%; FEV_1: –1.6; $FEF_{25–75}$: –2.6%, all $p<0.01$; n = 127) (Figure 2). Mean FVC remained low (–1.1%, $p < 0.02$) two hours after surfacing (n = 63). On the average, no significant differences from baseline remained five, 15 to 17 hours post diving, or on either of the days (Day +1 or Day +2) following a single dive (n = 33, 30, 26, and 26, respectively).

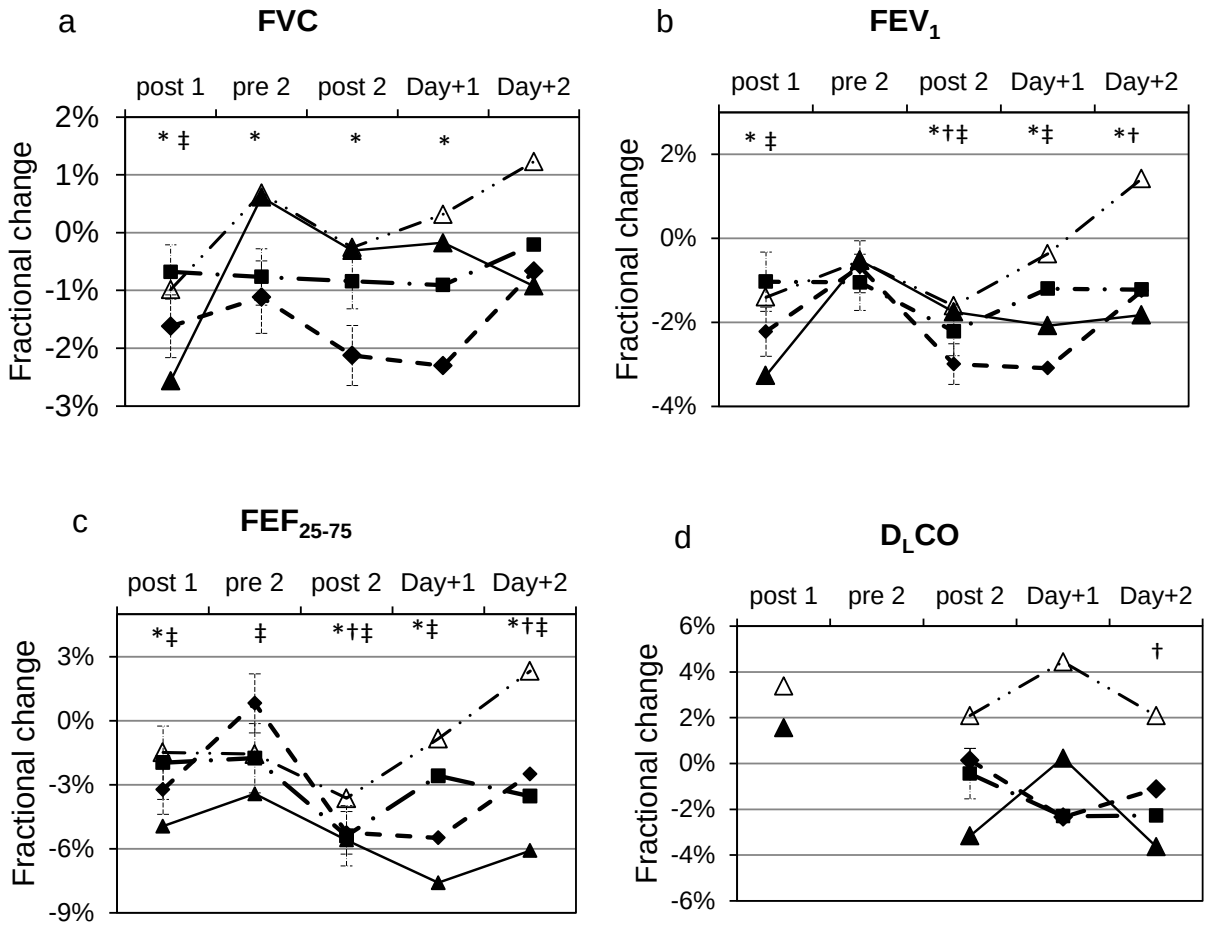

Figure 3. Changes from baseline as functions of time, means and standard errors. ─ ─◆─ ─: three-hour; ── · ── ■── · ──: six-hour;──▲── ──:15-hour SI; ── ·· ── Δ── ·· ──: 17-hour SI. Differences from baseline at top of panels ($p<0.05$): *Three hour, †six hour, ‡ 15-hour SI.

As noted below, the changes from baseline of FVC and FEV_1 after one dive, significant when all three-hour first dives and single dives were combined, were not significant for all subsets of first dives, specifically, not for the six- or 17-hour SI dive series. Conversely, the change from baseline of $FEF_{25–75}$ after a single dive, not significant

when all first and single exposures were combined, was significant in the three- and 15-hour SI.

For the three-hour SI dive series, mean FVC, FEV_1 and $FEF_{25–75}$ after the first dive differed from baseline ($p<0.01$, $p<0.01$, $p<0.02$, respectively) (Figs. 3a–3c), but before the second dive, only FVC differed from baseline ($p<0.04$) and not from the value after the first dive. Mean FVC was depressed after the second dive and on Day +1 (both $p<0.01$), but values did not differ significantly from those after the first dive. After the second exposure and on Day +1, mean FEV_1 and $FEF_{25–75}$ differed from baseline (all $p<0.01$) but not from the value after one dive. On Day +2, both FEV_1 and $FEF_{25–75}$ differed from baseline ($p<0.02$) but showed recovery, differing also from the value after the second dive (FEV_1: $p<0.01$, $FEF_{25–75}$: $p<0.03$).

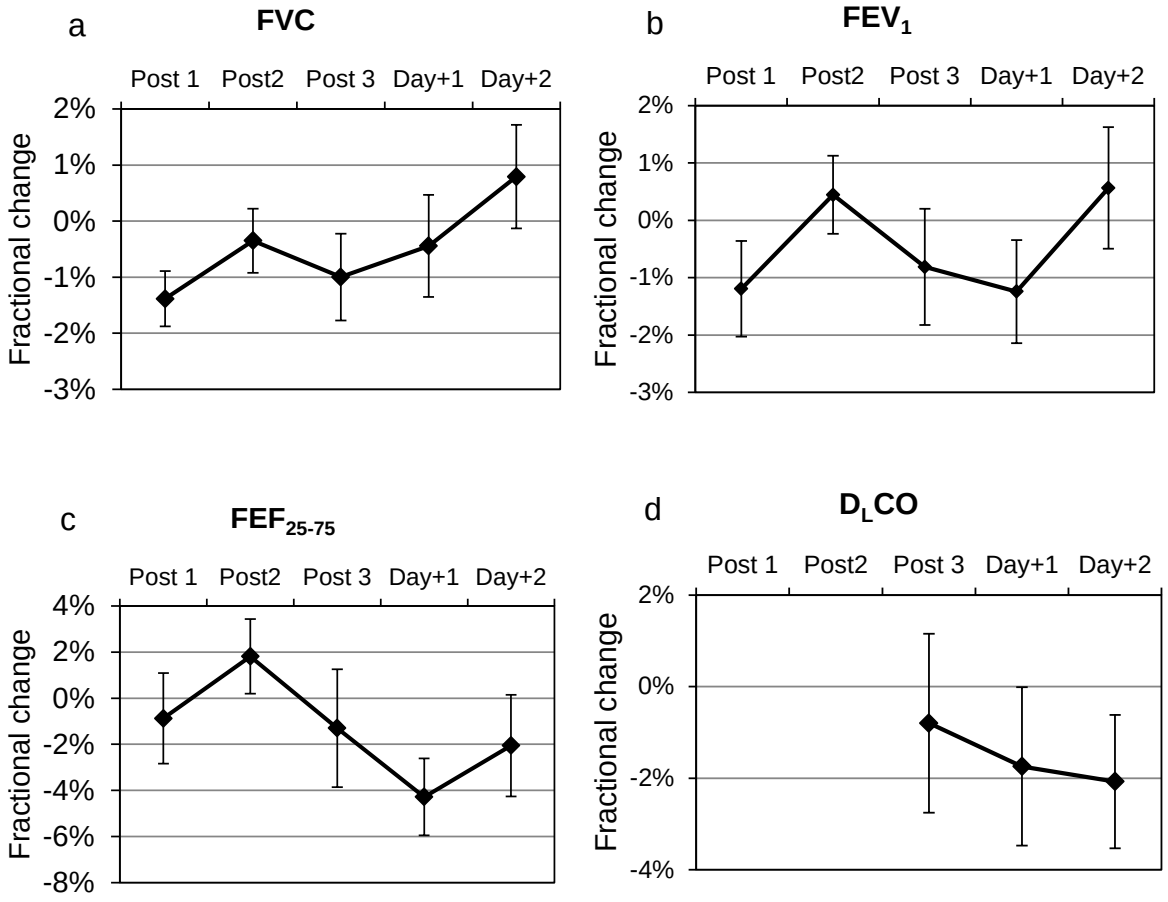

Figure 4. Changes from baseline as functions of time after three, 30-minute exposures with two-hour SI, means and standard errors.

For the six-hour SI series of exposures, none of the values differed from baseline after the first dive. Mean FVC (Fig. 3a) did not differ from baseline at any measurement, and FEV_1 and $FEF_{25–75}$ (Figs. 3b, 3c) were depressed only immediately after the second dive (both $p<0.02$). Mean D_LCO (Fig. 3d) was depressed on Day +2 ($p<0.05$).

When all overnight surface interval dives (both 15- and 17-hour) were considered as one dive series, FVC, FEV_1 and $FEF_{25–75}$ differed from baseline after the first dive ($p<0.01$, $p<0.01$, $p<0.02$, respectively), and FVC was below baseline before the second exposure ($p<0.04$). FVC and FEV_1 did not differ from baseline at any other measurement (Figs. 3a, 3b), but $FEF_{25–75}$ (Fig. 3c) was depressed after the second dive and on Day +1. If only data from the 15-hour SI group were considered, FEV_1 was below baseline after the second dive ($p<0.03$) and on Day +1 ($p<0.2$), as was $FEF_{25–75}$ after the second exposure and on both follow-up days ($p<0.02$). No values differed significantly from baseline for the 17-hour SI series, probably because of the small number of data (n=12).

After the 30-minute dives there were no changes on the average at any measured time (Figure 4).

INCIDENCES OF PULMONARY TOXICITY

Immediately post dive

The incidence of pulmonary oxygen toxicity at a measurement time is given by the fraction of the divers who have any symptoms or ΔPF at that point. Values obtained immediately after the second exposures are shown in Figures 5a (symptoms) and 5b (ΔPF) along with Agresti Coull (AC) 95% binomial confidence intervals.

Symptoms and ΔPF did not generally coincide, and symptoms were approximately three times as frequent as ΔPF. The duration of exposures to PO_2 = 130 kPa expected to yield similar incidences are shown on the right-hand axes of Figures 5a and 5b. Note that the confidence intervals given are those for the observations; they do not include uncertainties implicit in the conversion to equivalent exposure time.

Symptoms

The incidence of respiratory symptoms immediately after a single, three-hour exposure to PO_2 = 200 kPa was 15% (AC 95% CI 8% to 23%). After second exposures, incidences of symptoms (Figure 5a) increased significantly with three- and six-hour SI; for the combined 15- and 17-hour SI, the numerical increase from 15% to 30% was not statistically significant. However, the incidence of symptoms did not increase monotonically with decreasing SI as was anticipated. Incidence was very similar after the shortest and longest recovery time (three-hour and 15- or 17-hour SI), while that

after the intermediate six-hour SI was 52%, a difference from the three-hour SI that approached statistical significance ($p<0.07$ by Fisher's Exact Test).

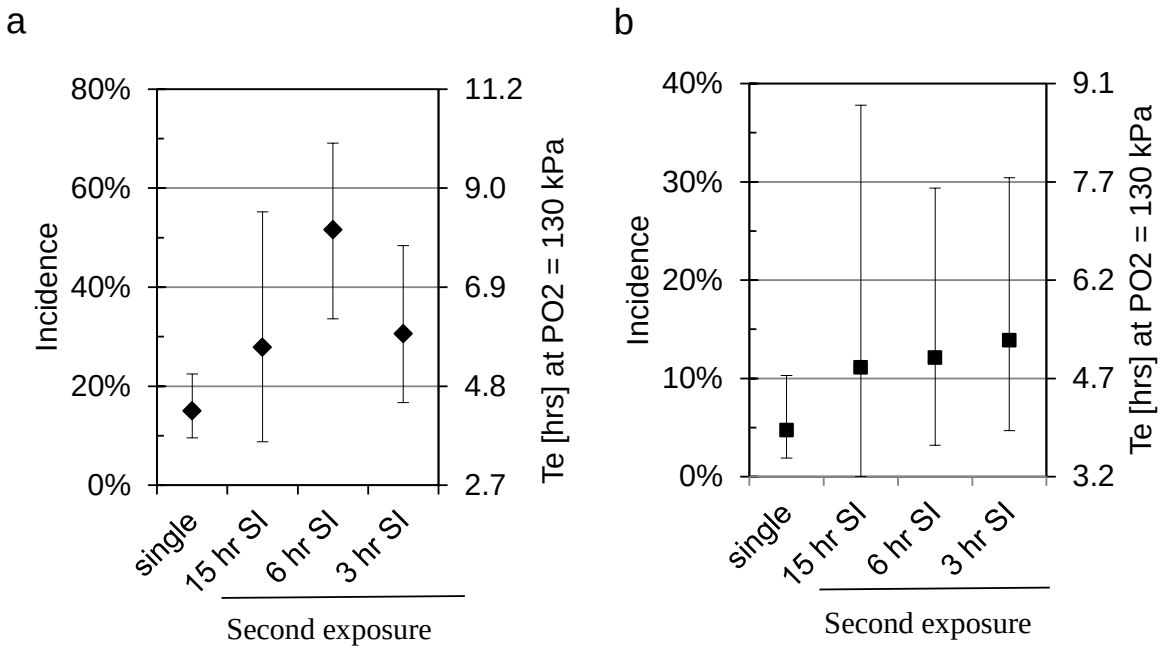

Figure 5. Incidences of symptoms of pulmonary oxygen toxicity immediately after exposure, a) symptoms, b) ΔPF. The vertical axis on the right gives equivalent time with PO_2 = 130 kPa (see text). Measured incidences and Agresti Coull binomial 95% confidence intervals are shown. Note the different scales for the two panels.

ΔPF

The incidence of ΔPF immediately after a single three-hour exposure to PO_2 = 200 kPa, was 5% (95% CI 0.4% to 10%) (Fig. 5b). No significant decrements in D_LCO were associated with the single three-hour exposures at any measurement time. Although the incidence of ΔPF after a second exposure increased numerically with decreasing SI, it reached only marginal statistical difference ($p<0.07$) from that after a single exposure, and that only after the three-hour SI (Figure 5b).

Time course of recovery, single dive

Figure 6 shows the time course of recovery after a single three-hour dive. Immediately after the exposure, the incidence of symptoms (Fig. 6a) was 15%, significantly different from zero ($p<0.01$) when all 127 exposures were considered. It dropped to 5% after two hours when data from 63 exposures were available, statistically different from that immediately after the dive by Fisher's Exact Test. However, incidence was 18% after five hours (n=33), and did not differ from that immediately for any of the later measurements.

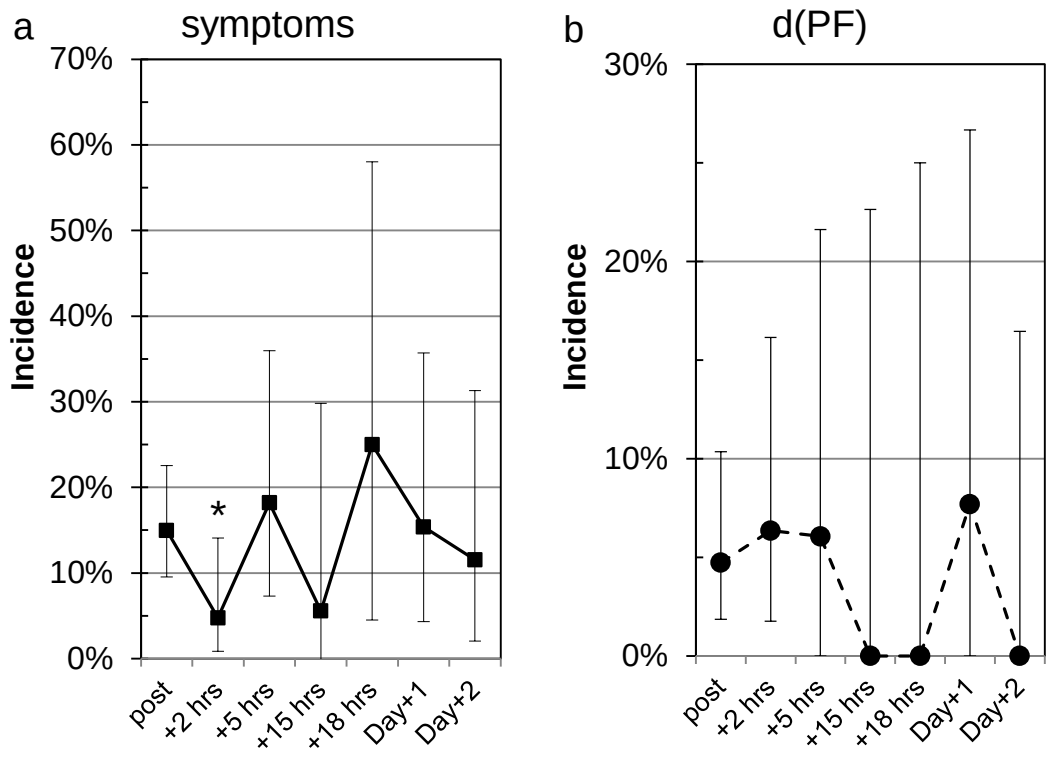

Figure 6. Incidences of pulmonary oxygen toxicity as a function of time after a single three-hour exposure. Bars represent Agresti-Coull 95% confidence intervals. a) symptoms; b) ΔPF.* indicates statistical difference from incidence immediately post dive ($p<0.05$).

The 5% incidence of ΔPF immediately after a single exposure (Fig. 6b) was statistically significant when all 127 exposures were considered. Although the incidence was essentially unchanged numerically two and five hours after surfacing, it was no longer different from zero at five hours (lower 95% CI approaches 0) because of relatively few measurements (n = 33). None of the later measurements differed from zero or from that immediately after surfacing because low numbers.

Time course of recovery, dive pairs

After second, three-hour exposures (Fig. 7a), the incidence of symptoms was significantly greater than zero immediately after diving and on Day +1 for all SI and on Day +2 for six- and 15-hour SI. Immediate incidence of symptoms for three- and six-hour SI (marginally – $p<0.06$ – for combined 15- and 17-hour SI) was greater than that immediately after single three-hour exposures, as was that on Day +1 for six-hour SI.

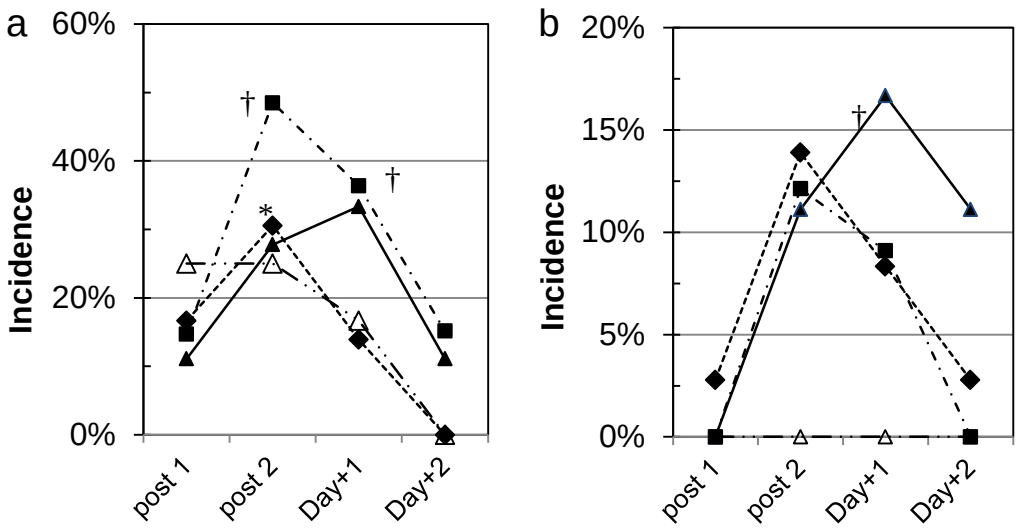

Figure 7. Incidences of pulmonary oxygen toxicity as functions of time after paired three-hour dives. Error bars omitted for clarity. Note the difference in scale for the two panels, a) Symptoms and b) ΔPF. "Post 1" is the incidence after the first exposure of the pair, and "Immed" replicates the data of Figure 5.

– –◆: three-hour SI, – · –■:six-hour SI, ——▲:15-hour SI, –·· –Δ: 17-hr SI. Different from post 1: *: three-hour SI differs, †: six hour SI differs. (Differences from zero not marked.)

After second exposures, the incidences of ΔPFs (Fig. 7b) were significantly greater than zero after three-hour SI immediately after surfacing, after six-hour SI on Day +1, and after 15-hour SI at all measurement points. D_LCO was depressed only on Days+1 and +2: after 15-hour SI in two subjects on Day +2; after six-hour SI, in three subjects on Day +1 and one on Day +2; and after three- hour SI, in two on Day +1 and two on Day +2.

Time course of recovery, 30-minute dives

After 30-minute dives with two-hour SI, symptoms were infrequent, with an incidence not different from zero. ΔPF, although also infrequent, increased with time and number of dives, to reach 11% on the day after diving (Fig. 8).

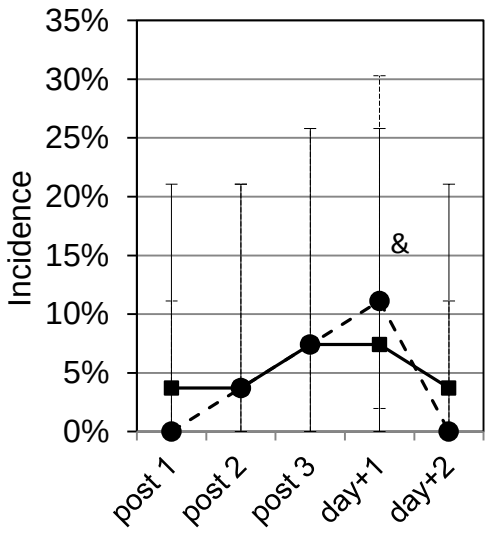

Figure 8. Incidences of pulmonary oxygen toxicity as a function of time after three 30-minute dives with two-hour SI. —■: symptoms; - - -•: ΔPF. &: Differs from 0 ($p<0.05$).

Other effects

No changes in visual refraction or acuity were observed across these exposures. One subject aborted his oxygen exposure with symptoms of hypercapnia. Another reported tingling and numbness of his head and face after 2 hours, 52 minutes of oxygen at 200 kPa, symptoms that probably represented central nervous system (CNS) oxygen toxicity. The symptoms resolved when he removed the hood to breathe chamber air. Although another two subjects reported symptoms consistent with CNS oxygen toxicity, because their symptoms did not resolve for more than 20 minutes after cessation of oxygen breathing or recurred later in the day, they were deemed not to be CNS toxicity.

DISCUSSION

Immediately after three-hour exposures to PO_2 of 200 kPa, pulmonary oxygen toxicity is mild but measurable, with a 15% probability of symptoms, and 5% probability of ΔPF and an average 1.2% decrease in FVC, 1.6% in FEV_1, and 2.6% in $FEF_{25–75}$. Similar incidences of ΔPF, though not similar average decrements in pulmonary function indices, are expected after 4.0 hours exposures to PO_2 = 130 kPa, and similar incidences of symptoms, after 4.3 hours at PO_2 = 130 kPa (4).

Exposures to PO_2 = 200 kPa provoke pulmonary oxygen toxicity faster than do exposures to PO_2 = 130 kPa, as is expected (12, 13). The single exposure results are also in concordance with those of Clark and Lambertsen (14), who reported that during exposure to PO_2 = 200 kPa symptoms began after three to eight hours, and vital capacity was measurably decreased in 9 of 11 subjects by the fourth hour. However, recovery from exposures to the two PO_2s was also expected to be similar or perhaps slightly faster from PO_2 = 200 kPa with its shorter exposure duration (12, 13). Thus, even after single three-hour exposures, the time course of symptom reports was slightly surprising; after 4.3 hours at PO_2 = 130 kPa the model based on that partial pressure would predict no recovery in the first few hours (4), but also no symptoms on Day +2.

Although the results from 30-minute dives are not conclusive, they suggest that the two-hour SI considered sufficient to avoid accumulation of CNS oxygen toxicity effects (5) does not permit complete recovery of pulmonary effects. If the SI is at least two hours, a U.S. Navy diver using an oxygen rebreather UBA is permitted to dive to 30 fsw for 80 minutes three times in a day, or, in principle, to 35 fsw for 25 minutes nine times. A diver repeating exposures to that extent could be expected to have some pulmonary effects. Perhaps the CNS washout times should also be reconsidered.

Simple inspection of the indices of pulmonary function and their average changes from baseline do not give a clear indication of recovery from pulmonary oxygen exposure. With the exception of FVC in the three-hour SI series, average values of the indices did not differ from baseline after the surface intervals (“pre dive 2”), yet the second dives for both three- and six-hour SI cause numerically greater average decrement than the first (Fig. 3), and second dives after three and six-hour SI were associated with greater incidence of symptoms than were first dives, a greater incidence that persisted to Day +1 (Fig. 7).

Second exposures following various SI were planned to measure rate of recovery in a manner similar to that previously used for PO_2 = 130 kPa (4). Tacit assumptions were 1) that exposure effects combine through linear superposition (as additive effects), and 2) that recovery begins at the end of exposure and is monotonic. In other words, the assumptions were 1) that the immediate effects of a second three hour exposure would be the same as the immediate effects of the first three hour exposure, implying that “three hour exposure effects” could be subtracted to yield residual effects from the first

exposure, and 2) that the incidence of symptoms and ΔPF seen after the second exposure would decrease or remain unchanged as the intermediate recovery time, the SI, increased. The second assumption can be modified to include delayed onset injury if recovery is monotonic once it begins.

The average pulmonary function indices showed greatest differences with the shortest SI and similar differences for the intermediate and longest SI (Fig. 3), but the incidences of symptoms were highest after the intermediate, six-hour SI (Fig. 7a). One explanation to consider is that delayed injury manifests itself after exposure, beginning sometime between six and nine hours into recovery. Clark and Lambertsen (13) saw continued decrement in vital capacity through the first 2 to 4 hours after a 10- to 12-hour exposure to 200 kPa, when average vital capacity was decreased by 10.3% and average FEV_1 by 9.3%. The data presented here show a trend toward lower mean $FEF_{25–75}$ in the period five to 22 hours (Day +1) after a single three-hour exposure (Fig. 2), depression of FVC and FEV_1 on Day +1 after single two-hour exposures (Fig. 2), and D_LCO decrements only on Days +1 and +2. However, after single three-hour dives, mean values (Fig. 2) did not indicate a large post-exposure decrease in pulmonary function indices, and incidences of symptoms and ΔPF (Fig. 6a) also did not increase. Further, after pairs of dives, the mean changes in pulmonary function were greatest after the three-hour SI, while six-hour SI and 15-hour SI were similar to each other. That evidence appears to exclude a simple delayed injury effect.

The interactions of later exposures with earlier ones appear to be non-linear. Our data do not allow for more than speculation as to cause, but one possibility is that inflammation might increase airways sensitivity to oxygen injury. Conversely, airway irritation causing cough, inspiratory burning, chest tightness, and dyspnea might not have affected measured pulmonary function (except by making the maneuvers less pleasant for the subjects, leading to the difference between symptoms and ΔPF apparent in Figures 5, 6a, and 7. The increase in symptoms to more than twice the incidence after a single exposure, though, brings to mind the unexpected incidence in divers of CNS symptoms during dives when PO_2 was approximately 156 kPa but an earlier short excursion3 had raised PO_2 to approximately 215 kPa (15).

This series of exposures does not include an air control. The doubled gas density of these experiments will have altered gas flow dynamics and may have promoted some airway irritation. However, flow-volume parameters have been shown to be unaltered after 14 to 30 days breathing a helium oxygen mixture with PO_2 = 40 to 60 kPa at total pressures of 3100 to 4600 kPa (30.6 to 45.4 ATA, or 980 to 1470 fsw) (16). Helium at 3100 kPa has similar density to air at 400 kPa, or about twice the density encountered in these experiments. Further, even if some of the symptoms relate to gas density, they are inescapably connected to breathing of 200 kPa of oxygen.

Hypercapnic episode

Hoods are considered an easy modality for administering oxygen in hyperbaric chambers. One of the divers in this study, though, reported feeling hot and flushed, was aware that his heart rate was high, and had difficulty concentrating on the card game he was playing. Because his hood had been overinflating, he had adjusted the flow to try to correct the problem. Symptoms abated when he removed the hood to breathe chamber air. In a follow-up unmanned test with a breathing simulator that "exhales" CO_2, inspired CO_2 in a hood on a manikin head was found to be elevated under all conditions, highly variable, and a strong function of inlet oxygen flow (11).

CONCLUSIONS

Some after-effects of a three-hour exposure to PO_2 of 200 kPa can linger for 15 hours, when a second three-hour exposure causes a significantly greater average decrease in FEF_{25-75} than that from a single exposure (Fig. 3). After a second three-hour exposure following a 15-hour SI, the incidence of symptoms (11%) remains significant two days later (Fig. 7a).

Because of the absence of linear system behavior, specifically the failure of the superposition (additivity) assumption, we are unable to derive a model to generalize from these exposures. We cannot differentiate, for example, between a six-hour SI and an SI twice the length of the exposure. Many more exposures with more SI and more specific measures of inflammation would be needed to tease out the answers. Further, we cannot assign meaningful equivalent times at PO_2 = 130 kPa to exposures from 200 kPa. However, we can caution that repeated exposures to PO_2 = 200 kPa can be more than additive in their negative effects.

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